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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,486	08/31/2006	John S. Yu	22862-0003US1 / 67789-567	6180
26161	7590	10/16/2009	EXAMINER	
FISH & RICHARDSON PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			JUEDES, AMY E	
			ART UNIT	PAPER NUMBER
			1644	
			NOTIFICATION DATE	DELIVERY MODE
			10/16/2009	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/598,486	YU ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 27 July 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 12-14 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 12-14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/27/09 and 12/21/07</u> .                                    | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

1. Applicant's amendment and remarks, filed 7/27/09, are acknowledged.  
Claims 1 and 3-7 have been amended.  
Claims 8-11 have been cancelled.  
Claims 12-14 have been added.  
Claims 1-7 and 12-14 are pending and are under examination.
2. Upon reconsideration, and in view of Applicant's amendments and remarks, the rejection of the claims under 35 U.S.C. 112 first paragraph is withdrawn.
3. The rejection of the claims under 35 U.S.C. 103 is withdrawn in view of Applicant's amendment to limit the claims to methods of treating cancer in a "human".
4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7 and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/38730 (of record), in view of Geiger et al., 2001, and Kalinski et al., 1998 (of record) as evidenced by the material safety data sheet for NS-398 (2008).

WO 00/38730 teaches a method of treating cancer in a human subject comprising administering a combination of a COX-2 inhibitor and a vaccine to the subject (see page 9, in particular). WO 00/38730 teaches that the method is suitable for treating a wide range of cancers including ependymal tumors, glioblastoma (i.e. glioma or brain cancer), and neuroblastoma (see page 10, in particular). WO 00/38730 teaches that the vaccine includes agents that induce the patients immune system to mount an immune response against the tumor, and that the COX-2 inhibitors include celecoxib and N-[2-(cyclohexyloxy)-4-nitrophenyl] methanesulfonamide (see page 22, 42, and 52, in particular). As evidenced by the material safety data sheet, N-[2-(cyclohexyloxy)-4-nitrophenyl] is NS-398. WO 00/38730 teaches administering a single dose of the COX-2 inhibitor at a concentration of 1mg to about 1000mg (see page 66, in particular). WO 00/38730 also teaches that COX-2 inhibitors function to treat cancer by inhibiting the COX-2 activity of neoplastic lesions, since the products of COX-2 activity, such as PGE<sub>2</sub>, stimulate cancer cell growth and inhibit immune surveillance (see page 36-38, in particular). WO 00/38730 also teaches that the combination therapy can maximize the therapeutic effect of each of the compounds (i.e. the COX-2 inhibitor enhances the effect of the vaccine, see page 11-12, in particular).

WO 00/38730 does not teach administering a dendritic cell as the vaccine component.

Geiger et al. teach that dendritic cells can be used as a vaccine to induce an immune response and treat cancer in human patients, including those with neuroblastoma or primitive neuroectodermal tumor (see page 8515, in particular). Geiger et al. teach that the administered dendritic cells are immature dendritic cells that have been pulsed with tumor lysate in vitro (see page 8515, in particular). Geiger et al. teach administering  $1 \times 10^7$  dendritic cells (see page 8515, in particular). Geiger et al. also teach that injected dendritic cells may mature in vivo after administration (see page 8517, in particular). Geiger et al. also teach that IFN-gamma production (i.e. a Th1

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response) correlates with vaccine efficacy (see page 8518, in particular). With respect to claims 12 and 13 of the instant application, it is noted that the instant specification does not specifically define the terms "primed" or "unprimed". Rather, the specification on page 12 states that dendritic cells can be "primed" ex vivo by conventional methods for example loading with a tumor cell lysate. The specification further states that "unprimed" dendritic cells include those dendritic cells that do not rely upon acquisition of tumor tissue as a protein source, and the subsequent culturing therewith. Thus, the specification only gives antigen pulsed dendritic cells as a specific examples of "primed" dendritic cells, and dendritic cells not cultured with antigen as a specific example of "unprimed" dendritic cells, but does not specifically define the scope of the terms "primed" and "unprimed". It is noted that Geiger et al. teach pulsing the dendritic cells with tumor cell lysate, and thus said dendritic cells can be considered "primed" with antigen. However, Geiger et al. also teach that the dendritic cells are immature dendritic cells that have not been actively matured in culture with specific maturation factors (see page 8516, in particular). Given the broadest reasonable interpretation of the term "unprimed" it can be considered to encompass immature dendritic cells which have not been treated or primed in vitro with maturation factors (i.e. the dendritic cells of Geiger et al. are "unprimed" with respect to maturation factors).

Kalinski et al. teach that PGE-2 impairs IL-12 production and Th1 priming capacity of dendritic cells if it is present when dendritic cells are undergoing maturation (see page 2807 and 2808, in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a dendritic cell as the vaccine, as taught by Geiger et al., in the method of treating cancer of WO 00/38730. The ordinary artisan at the time the invention was made would have been motivated to do so and have a reasonable expectation of success, since Geiger et al. teach that dendritic cells can be used as a vaccine for treating cancer. Furthermore, WO 00/3870 teaches that inhibition of COX-2 decreases PGE-2 production, and Kalinski et al. teach that PGE-2 inhibits IL-12 production and TH1 priming by dendritic cells. Thus, the ordinary artisan would be motivated to administer a combination of a COX-2 inhibitor with a dendritic cell vaccine

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to inhibit PGE-2 production in order to enhance IL-12 production and Th1 priming by the dendritic cells in vivo.

5. No claim is allowed.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 7am to 3:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amy E. Juedes

Patent Examiner

Technology Center 1600

/Amy E. Juedes/

Patent Examiner, Art Unit 1644